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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,102	05/01/2001	Dennis A. Carson	220002062900	5759

7590 10/24/2006

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,102	CARSON ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/22/2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,16,28 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,16,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f)..

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8, 16, 28, and 29 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112, Maintained

Claims 1-8, 16, 28, and 29 **remain rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn because applicant's argument is persuasive. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

This new matter rejection is because of the limitation added in the amendment filed on 06/04/2005, i.e. "the antibody inhibits growth of the malignant cell that expresses the frizzled 5 receptor" in claims 1, and 16, the limitation "wherein the antibody is effective for immunotherapy of a malignant cell that overexpresses the frizzled 5 receptor" in claim 28.

Applicant argues that the support is in original claims 1 and 10. This argument has been fully considered but found unpersuasive. Although original claims 1 and 10 have support for an antibody binding to SEQ ID NO: 68, and modulates a biological activity of a malignant cell that express a frizzled 5 receptor, the specification as originally filed does not have support for the antibody inhibits growth of the malignant

cell, or" antibody is effective for immunotherapy of a malignant cell that overexpresses the frizzled 5 receptor"

Claim Rejections - 35 USC § 103

Claims 1-8, 16, 28, and 29 rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al (IDS, #1711998, Proc. Natl. Acad. Sci. USA. vol. 95, pages 10164-9) in view of US Pat. 5,677,171 (IDS, Hudziak et al., Oct. 14, 1997).

Claims 1-8, 16, 28, and 29 are drawn to a purified antibody binds to an epitope at the N-terminal extracellular domain (SEQ ID NO: 68) or pharmaceutical comprising said antibody, wherein the antibody inhibits growth of a malignant cell expressing a frizzled 5 receptor.

Applicant argues that the invention is based on the recognition that frizzled 5 is overexpressed in some cancers, thus can be used as tumor specific antigens and the claimed antibodies are immunotherapy agents used to inhibit growth of cancer cells. This argument is not persuasive because applicant argument is not commensurate in scope of the claims. The specification at page 25 (Examples 1 and 2) discloses that frizzled 2 is overexpressed in cancer cells, while frizzled 5 is expressed both in normal and cancer cells (see Table III). In addition, Examples 3-6, at beginning page 26 of the specification discloses anti-frizzled 2 antibody inhibits growth of cancer cells. The claimed invention is drawn to antibody to frizzled 5, not frizzled 2.

Applicant argues that none of the cited references provide evidence that the frizzled 5 protein is overexpressed in malignant cells or that antibodies directed against are useful to kill cancer cells. Applicant argues the Office assumes that all wints and

frizzled proteins have assigned function, and this assumption is incorrect. Applicant argues with Exhibit A (Wong et al), which shows that wnt 5a had no transforming activity. These arguments have been fully considered but found unpersuasive. As stated in the previous Office action, Tanaka et al., teach (note page 10164, right column under the heading Cloning of the Human FZ Genes, and also page 10165, left column under the heading "Identification of Human Esophageal Carcinoma-Specific Fz Gene) that the frizzled 5 receptor protein comprising instant SEQ ID NO: 68 is isolated from a human esophageal carcinoma tissue. Note the sequence alignment provided with the Office action mailed on 08/04/2003. This clearly indicates that a malignant esophageal cell express the human frizzled 5 protein. Tanaka et al., at the paragraph bridging pages 10164-5 teach that N-terminal extracellular domain of a frizzled receptor lies just before the first transmembrane helix, also teach "the ectodomain of Fz functions as natural antagonist of Fz-mediated signal transduction". Tanaka et al., at page 10164 teach Wnt binds to Frizzled family of seven-transmembrane proteins, and the seven-transmembrane proteins frizzled family proteins act as receptors for "Wnt oncoprotein" (see page 10164, left column) This suggests frizzled member proteins in tumor development and importance of extracellular domain of frizzled receptor for receptor-mediated signal for wnt-mediated oncogenic process. This disclosure is similar to the instant specification, which show a member of frizzled protein (i.e. frizzled 2) being involved in the development of cancer.

Applicant argues that Hudziak patent does not suggest that any protein with an extraceullar ligand binding domain is suitable candidate to raise antibodies, and provide

no motivation or expectation of success that antibodies against fzdt would inhibit growth of malignant cells. This argument has been fully considered but found unpersuasive. Hudziak patent teaches at column 5, lines 16 and 17, "antibodies to inhibit the growth of tumor cells"; at column 6 lines 5-13 "Advantageously antibodies are selected which greatly inhibit the receptor function by binding the steric vicinity of the ligand binding site of the receptor (blocking the receptor), and/or which bind the growth factor in such a way as to prevent (block) the ligand from binding to the receptor. These antibodies are selected using conventional in vitro assays for selecting antibodies which neutralize receptor function." This suggests that an antibody binding to extracellular domain, where the natural ligand binds to, would inhibit the function of the receptor. Hudziak patent also teaches assays to screen an antibody that inhibits growth of the malignant cell. Hudziak patent teaches a cytotoxic response and label at claims 1-39.

Therefore one of ordinary skill would have been motivated to screen an antibody binding to the extracellular domain (i.e. the natural ligand binding site) of frizzled 5 protein, which is expressed on a malignant cell as taught by Tanaka et al., wherein the antibody inhibits the growth of the malignant cells since the screening assay is taught by Hudziak patent. It would have been obvious to one of ordinary skill in the art to make and use an antibody directed the extracellular domain of a receptor because of the advantage as taught by the Hudziak patent. Further, one of ordinary skill would be motivated to screen an antibody inhibiting cancer cells because this kind of antibody could be used in cancer treatment as taught by Hudziak patent, and cancer treating antibody would make money.

In addition, based on Noelle v. Lederman, 69 USPQZd 1508, 1514 (Fed. Cir. 2004), an antibody to known antigenic sequence is obvious, and one of skill would have been arrived at the claimed invention with a reasonable expectation of success, given the amino acid sequence has been known, the extracellular domain of a frizzled 5 is where the natural ligand binds to, had been well known in the art before the effective filing date of the instant application as taught by Tanaka et al., and also given that advantage of the antibody to extracellular domain and an assay to isolated an antibody inhibiting the growth of a malignant cell had been known in the art as taught by Hudziak patent well before the effective filing date of the instant application.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

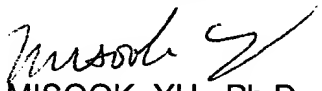
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642